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FOLEY & LARDNER
402 WEST BROADWAY
23RD FLOOR
SAN DIEGO, CA 92101

EXAMINER	
GABEL, GAILENE	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 31

Application Number: 09/349,194
Filing Date: July 07, 1999
Appellant(s): BEUCHLER et al.

Barry Wilson
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed September 8, 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 85-87 and 114-118 stand or fall together, claims 88-90 and 119-123 stand or fall together, claims 91-

93 and 124-128 stand or fall together, claims 94-96 and 129-132 stand or fall together, claims 102-106 stand or fall together, 139 stands alone, and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

No prior art is relied upon by the examiner in the rejection of the claims under appeal.

(10) Grounds of Rejection

Appellant's request for reconsideration of the objection made to claims 114-118 and 139 under 37 CFR 1.75 as being a substantial duplicate of claims 102-106 and 138, is persuasive and has been withdrawn. Accordingly,

The following grounds of rejection are applicable to the appealed claims:

Claims 85-96, 102-106, and 114-133 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for an assay for determining free and complexed cardiac specific isoforms of troponin (cTn) using a cocktail of antibodies, each having specific binding for free cTnI, binary complex of cTn, and ternary complex of cTn, does not reasonably provide enablement for an assay for determining free and complexed cTn using an

antibody, i.e. single antibody, having specific binding for each and all of free cTnI, binary complex of cTn, and ternary complex of cTn. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is set forth in prior Office Action, Paper No. 25.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for determining the presence or amount of each and all of free and complexed isoforms of cTn using a cocktail of antibodies having specific binding for each and all of free, binary complex, and ternary complex isoforms of cTn.

The state of the prior art- the prior art of record fails to disclose a method for determining the presence or amount of all free, binary and ternary complexed isoforms of cTn using an antibody having specific binding for each and all of the free, binary, and ternary complexed isoforms of cTn.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the presence or amount of all of the free, binary and ternary complexed isoforms of cTn in a sample can be determined using an antibody wherein the antibody has specific binding for each and all of the free, binary, and ternary complexed isoforms of cTn.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to determine the presence or amount of all of the free, binary and ternary complexed isoforms of cTn in a sample using a cocktail of antibodies that have been generated to specifically bind one of the free, binary, and ternary complexed isoforms of cTn. However, the specification fails to provide any guidance to enable the claimed method to make and use an antibody that specifically binds all of the free, binary and ternary complexed isoforms of cTn in a sample to determine the total concentration of a cTn isoform.

The presence or absence of working examples- working examples are provided in the specification that show that all of free and complexed isoforms of cTn can be determined in a sample using a cocktail of antibodies that specifically bind each of the free, binary, and ternary complexed isoforms of cTn. There are no working examples that show analogous results using an antibody, which is encompassed by the broad scope of the instant claims.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method that is capable of determining the presence or amount of all free, binary, and ternary complexed isoforms of cTn. As recited, the instant method is capable of determining the presence or amount of all of free, binary, and ternary complexed isoforms of cTn using a single antibody that has specific binding for each of the free, binary, and ternary complexed isoforms of cTn.

In this case, the specification at pages 6-7 describes antibodies for use in the claimed method that are monoclonal, polyclonal, fragment thereof, and recombinant . These antibodies are characterized as being "sensitive" or "insensitive", the sensitive antibodies tend to bind and exhibit preferential detection of a single form of troponin and the insensitive antibodies tend to bind and exhibit detection of more than one form of troponin. In pages 13-14, the specification shows that an insensitive antibody is utilized to bind to the free and complexed forms of troponin; that is, insensitive with respect to the oxidized, reduced, and complexed forms of troponin. Alternatively, more than one sensitive antibody would be necessary to measure both the free and complexed forms of troponin. At pages 21-22, the specification shows how to generate and select antibodies that are sensitive or insensitive to the binding of free troponin I or T, troponin I or T in binary complexes, and troponin I or T in ternary I/T/C complexes; this is accomplished by purification of free troponin I or T, binary troponin I/T, T/C, and I/C complexes and ternary I/T/C complexes, respectively, then injection into mice or rabbits to generate monoclonal or polyclonal antibodies. The antibodies are then screened for affinity and specificity with the

purified free troponin, binary complexes of troponin, and ternary complexes of troponin.

While the specification at pages 29-31 exemplifies using selected antibodies, i.e. a cocktail of antibodies, that bind each of free cTn, binary complexed cTn, and ternary complexed cTn, in the claimed method of determining the amount of free, binary complexed, and ternary complexed cTn, the specification does not show any working examples of the claimed method that would have successfully used one antibody that has specific binding for each and all of the free cTn, binary complexed cTn, and ternary complexed cTn. The fact that insensitive antibodies that bind more than one form of cTn has been characterized, is not sufficient to enable the breadth of the claimed method to use a single insensitive antibody in an assay to determine the presence or amount of all of free cTn, binary complexed cTn, and ternary complexed cTn. The specification does not establish a direct correlation between using a cocktail of insensitive and/or sensitive antibodies and a single "insensitive" antibody, which would lead the skilled artisan to say that the claimed method works for a single insensitive antibody to enable the breadth of the claimed method. The specification does not provide any teaching that suggests that an antibody generated against purified free cTn, an antibody generated against purified binary complexed cTn, or an antibody generated against purified ternary complexed cTn, has been successfully characterized to bind a conserved epitope for each and all of said free cTn, binary complexed cTn, and ternary complexed cTn in a sample. Further, the working examples at Example 15 and Example 16,

utilize a cocktail of antibodies to determine the presence or amount of all of free cTn, binary complexed cTn, and ternary complexed cTn in a sample. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan, a level of success and predictability, so as to enable the breadth of the claimed method. This is not the case in the instant specification. Thus, the claimed method is only enabled for use with a cocktail of antibodies having binding specificity for each of free cTn, binary complexed cTn, and ternary complexed cTn.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method using a single antibody, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method would work using a single insensitive antibody; 3) there is no proper guidance that shows that a single insensitive antibody has been successfully generated, characterized, and selected to bind each and all of free cTn, binary complexed cTn and ternary complexed cTn, 4) the nature of the invention is a method capable of determining the presence or amount of all forms, i.e. free and complexed, of cTn using a cocktail of antibodies, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that shows successful generation, characterization, and selection of an antibody that has

specific binding for each and all of free cTn, binary complexed cTn, and ternary complexed cTn , and lastly 7) the claims broadly recite a method for determining the presence or amount of all free and complexed forms of cTn using a single antibody that has specific binding for each and all of the free and complexed forms of cTn, without specifically stating how this can be done without undue experimentation.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

(11) Response to Argument

A) Appellant contends that use of the term "antibody" is enabled because the term "antibody" encompasses both monoclonal antibodies and polyclonal antibodies. According to Appellant, polyclonal antibody is by definition, a mixture of different monoclonal antibodies. Appellant, therefore, argues that the specification is enabled since Examiner has indicated that the instant specification is enabled with respect to a pool of antibodies, which requires that a polyclonal antibody of the claims would similarly be enabled.

In response, the claims recite "an antibody" which encompasses both "monoclonal antibody" and "polyclonal antibody". The recitation of "an antibody" does not exclude monoclonal antibody. Contrary to Appellant's argument, a polyclonal antibody is not a mixture of different monoclonal antibodies. A monoclonal antibody or monoclonal antibodies are antibody molecules having common specificity. A polyclonal antibody or polyclonal antibodies are antibody

molecules having different specificities. The definition of polyclonal antibody is thus, contradictory to Appellant's claim to "an antibody which *specific binds to* cTn in free cTn form, cTn in binary form complexed with troponin I or troponin C or troponin T, and cTn in ternary form complexed with two other troponin components selected from troponin I or troponin C or troponin T. Appellant's claims are drawn to "an antibody" that has a requisite common specificity to the conserved epitope common to each and all of the free cTnI, cTnI in binary form complexed with troponin I or troponin C or troponin T, and cTn in ternary form complexed with two other troponin components selected from troponin I or troponin C or troponin T. Accordingly, for the specification to be enabled, it is required to provide a teaching that suggests an antibody to be *monoclonal* that is generated against purified free cTn, an antibody that is generated against purified binary complexed cTn, or an antibody that is generated against purified ternary complexed cTn, and that has been fully and successfully characterized to bind one common specific *conserved epitope for each and all of the free cTn, binary complexed cTn, and ternary complexed cTn*. All the working examples provided in the specification utilize a cocktail of antibodies to determine the presence or amount of all of free cTn, binary complexed cTn, and ternary complexed cTn in a sample; thus, Appellant's instant specification is not enabled for the claimed invention.

B) Appellant submits that the Beuchler declaration is evidence that must be considered and that Examiner has failed to weigh the evidence as a whole, a consideration that is fundamental in any determination of enablement.

In response, the Beuchler declaration, having been substantially considered in previous responses, is an opinion declaration of Appellant as an interested party; thus, the Beuchler declaration is of reduced scientific probative value.

C) Appellant argues that Examiner has dismissed the declaration on the basis of an improper evidentiary standard, which requires actual data to prove enablement.

In response, both of Appellant's disclosure and declaration provide information that is prophetic in nature and state speculations in place of factual evidence meet evidentiary standard to support the claims. Evidentiary standard, to be proper, requires that experimentation is undue by showing predictability and success, i.e. by generation or production of the "one antibody" having the requisite common specificity as recited in the rejected claims, in addition to direction or guidance presented in making such antibody. Presence of working examples, also show success and/or that only reasonable quantity of experimentation is necessary, to enable Appellant's disclosure. Neither the disclosure nor the declaration fail to meet evidentiary standards as set for in In re Wands.

D) Appellant argues that Examiner applied an improper legal standard for judging compliance with enablement requirement since the presence of working examples is one consideration but is not the single determinative consideration.

In response and as set forth in In re Wands, enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Undue experimentation requires predictability and success in addition to direction or guidance presented, both of which are absent in Appellant's disclosure. Presence of working examples, also show success and/or reasonable quantity of experimentation necessary, but is also lacking in Appellant's disclosure. To reiterate, the specification at pages 29-31 exemplifies using a cocktail of selected antibodies, that bind each of free cTn, binary complexed cTn, and ternary complexed cTn, in the claimed method of determining the amount of free, binary complexed, and ternary complexed cTn. However, the specification does not show any working examples of the claimed method that would have successfully used one antibody that has specific binding for each and all of the free cTn, binary complexed cTn, and ternary complexed cTn. The fact that insensitive antibodies that bind more than one form of cTn, have been characterized, is not sufficient to enable the breadth of the claimed method to use a single insensitive antibody in an assay to determine the presence or amount of all of free cTn, binary complexed cTn, and ternary complexed cTn. Additionally, the specification does not provide any teaching that suggests that an antibody generated against purified free cTn, an antibody

generated against purified binary complexed cTn, or an antibody generated against purified ternary complexed cTn, has been successfully characterized to bind a conserved epitope for each and all of said free cTn, binary complexed cTn, and ternary complexed cTn in a sample. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan, a level of success and predictability, so as to enable the breadth of the claimed method. This is not the case in the instant specification.

E) Appellant argues that Examiner's interpretation of the meaning of "an antibody" as a single antibody, is without support of any evidence of record.

In response to Appellant's argument, which appears to intend excluding claiming to "a single antibody", it has been noted that use of the phrase "a single antibody" denotes a singular type or form of an element and does not *necessarily* imply a population, i.e. antibodies. This interpretation is analogous to Appellant's own claim recitations in Appellant's related Application under Appeal, Application Serial Number 09/687,051, which recites "selecting one *or more* antibodies ..." in claim 81 and "one *or more* antibodies" in claim 79. Thus, the phrase "or more" provides evidentiary confirmation in Appellant's disclosure(s) that "an antibody" is intended as one or single antibody.

F) Appellant argues that in addition to the specification, Appellant submitted a declaration of Dr. Beuchler as evidence of predictability, describing

why the skilled artisan would reasonably believe that the claimed antibody *could* be obtained.

In response, statements in Appellant's arguments such as "antigenic sites *may* remain available for antibody binding, ... and *may* be used to bind a free cardiac specific troponin isoform ...", "antibodies ... would be *expected to bind* ..., would also be expected to be available", and "even a monoclonal antibody *could* be produced having the requisite specificity", as well as statements in the declaration specifically in paragraphs 3, 4, 5, and 6 such as "can be performed", "regions may be present", "may obscure one or more cardiac specific regions ... may remain accessible ... antibodies may thus be selected ...", provide speculations which fail to provide factual evidence for the record and only confirm the prophetic nature of the disclosure. To reiterate, enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Undue experimentation requires predictability and success, that it has been successfully made, i.e. submission of a hybridoma cell that produces the "an antibody" that has specific binding for the conserved epitope for each and all of said free cTn, binary complexed cTn, and ternary complexed cTn, in addition to direction or guidance presented, both of which are absent in Appellant's disclosure and declaration. Presence of working examples using the "an antibody", also show success, i.e. that it has been successful, and that only reasonable quantity of experimentation is necessary, both of which are lacking in Appellant's disclosure and declaration.

For the above reasons, it is believed that the rejections should be sustained.

Claims 134-142 are allowable.

Respectfully submitted,

Gailene R. Gabel
November 25, 2003

Conferees
Long V. Le
James C. Housel

SPE AU 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

FOLEY & LARDNER
402 WEST BROADWAY
23RD FLOOR
SAN DIEGO, CA 92101